REMARKS

The present reply is submitted in response to the Office Action dated December 19, 2008. It is Applicants' understanding that claims 4 (2nd instance) – 16 have been renumbered as claims 5 – 17 per the previous response dated October 29, 2008, and based on the Office Action Summary page and the Examiner's comments on page 2 of the current Office Action. As such, Applicants refer to the renumbered claims 5 – 17 in the current response. In the Office Action, the Examiner indicated that claim 1 was rejected under 35 U.S.C. 102(b) over U.S. Patent No. 5,458,785 to Howe et al. ("Howe") and WO 2001/05510 to Kreuwel et al ("Kreuwel"). However, the rejection appears under the 35 U.S.C. § 103(a) heading, and the language of the rejection appears to indicate that an obviousness rejection was made under § 103(a). In addition, renumbered claims 15 – 17 were rejected under 35 U.S.C. § 102(b) as being anticipated by Howe and Kreuwel. Through this response, Applicants have canceled previously withdrawn claims 2-14 without prejudice. Applicants reserve the right to file continuation and divisional applications pursuant to 35 U.S.C. §§ 120 and 121 for the canceled subject matter. In addition, Applicants have amended claims 1, 15, 16, and added new claims 18 – 32. No new matter has been added, and support may be found, for example, in paragraphs 0215 – 0222, and Figs. 35A-F. Applicants respectfully request reconsideration of the application in view of the amendments made and remarks that follow, and respectfully submit that the application is in condition for allowance.

The Examiner rejected claim 1 either under 35 U.S.C. 102(b) or 35 U.S.C. 103(a) or both as anticipated and/or obvious over Howe and Kreuwel. Claims 15-17 were rejected as anticipated by Howe and Kreuwel. Applicants respectfully traverse these rejections, and submit that the claims are in condition for allowance.

Howe discloses a method for resuspending magnet particles. As disclosed by Howe, a magnet system attracts magnetically attractable particles into an annular ring pellet near the bottom end of a vessel. This conformation enables a pipette to be inserted through the center annulus of the pellet to the bottom of the vessel, and allows the pipette to fully drain the pellet by removing the supernatant from the vessel (see Col. 2, ll. 60-65, Col. 5, ll. 33-41). Thereafter, the pellet is resuspended by adding liquid to the vessel. After adding the resuspension liquid, Howe discloses drawing the annular pellet down to the bottom of the vessel and positioning the pipette a short distance above the pellet (see Col. 3, ll. 7-10, Col. 5, ll. 41-45). The magnetic field is then removed, and the pipette repeatedly draws the resuspension liquid into the pipette and expels the liquid from the pipette a number of times to resuspend the particles (see Col. 3, ll. 2-5, Col. 5, l. 41).

Kreuwel discloses a method of mixing magnetic particles in a vessel during a washing or elution step by moving magnets to drag the particles back and forth in opposite directions within the vessel. After this washing procedure, the magnetic particles are captured on the vessel wall and the wash liquid is removed from the container by a pipette. The vessel is then filled with fresh elution buffer. Subsequently, the magnetic particles are moved down to the extreme lower end of the vessel by moving the magnets. Elution buffer is then removed from the vessel leaving behind a required volume of elution buffer for release of nucleic acid from the particles. At the extreme lower end of the vessel, the buffer and particles are heated to activate the buffer to release the nucleic acid from the particles. After heating, the particles are dragged upwards to a position above the surface of the elution buffer, which physically separates the particles from the buffer. Thereafter, the elution buffer may be removed or additional liquid may be added to the vessel (see page 4, lines 1-6, page 6, lines 5-27, page 7, lines 28-32, page 8, and Fig. 4).

Unlike the Howe and Kreuwel references, Applicants' pending claims recite a method of separating magnetic particles from a fluid that utilizes two separate aspiration steps that are conducted on the same fluid held in the container at different locations, which in turn acts to ensure high capture of particles and reduce the loss of particles during separation of the fluid from the magnetic particles. As discussed in more detail below, the prior art made of record fails to disclose, teach, or suggest separating magnetic particles from fluid using at least two aspiration steps on the **same** fluid at the locations and in the manner claimed. Rather, the prior art made of record discloses methods which utilize a single aspiration step to remove a fluid from a container, and then subsequently adds another fluid to the container. This second fluid is then subjected to additional processing steps that also do not disclose, teach, or suggest, the method now claimed. Accordingly, Applicants respectfully submit that the pending claims are in allowable form, and respectfully request that the application be passed to issue.

Claim 1 of the present application has been amended to remove a redundancy in the claim. Claim 1 recites a method for separating magnetic particles in a fluid that includes, among other things, aspirating a preselected quantity of fluid from a first aspiration zone in the container, wherein the preselected quantity is less than 1/2 (one-half) the volume of the fluid residing in the container. Claim 1 also recites aspirating the fluid from a second aspiration zone whereby the magnetic particles are separated from the fluid. In this way, the present invention performs a volume reduction in a single container in a timely fashion, while ensuring high capture of particles for subsequent steps that are completed at relatively low volumes. The present invention allows more effective evacuation of fluid from the container, and the high capture of particles reduces the extent of magnetic particle loss during the aspiration of the fluid from the container.

As recognized by the Examiner, neither Howe nor Kreuwel disclose, teach, or suggest aspirating a preselected quantity of fluid from a first aspiration zone in the container, wherein the preselected quantity is less than 1/2 (one-half) the volume of the fluid, and aspirating the fluid from a second aspiration zone. Thus, a rejection under 35 U.S.C. 102(b) cannot stand because neither reference discloses each and every claim limitation. In order to cure this deficiency, the Examiner contends that it would have been obvious in either Howe or Kreuwel to aspirate various quantities of fluid to see what quantity most efficiently separates the magnetic particles suspended in the fluid in either Howe or Kreuwel. However, no reference(s) have been cited in support of the Examiner's obviousness contentions. Applicants respectfully traverse this rejection.

Howe teaches to **fully drain** magnetic particles formed into an annular ring pellet near the bottom of a vessel by removing supernatant fluid from the container. Thereafter, a resuspension liquid is added to the container. The pellet is then drawn to the bottom of the vessel, and a pipette is positioned to eject resuspension liquid at the pellet. The pipette repeatedly removes and adds the resuspension liquid back into the container to resuspend the magnetic particles in the fluid. (see Col. 2, ll. 60 – Col. 3, l. 7). Thus, any amount of resuspension liquid removed during resuspension is added back to the container during the Howe process, and **not** separated from the particles. In addition, after the initial resuspension liquid is ejected at the pellet, the magnetic field is removed and subsequent removal steps in Howe would include removal of magnetic particles and resuspension liquid, in order to effectuate resuspension of the particles in the liquid.

Conversely, the present invention of claim 1 is directed to a method of separating magnetic particles from a fluid, which reduces the loss of particles from the container during aspiration of fluid from the container. Therefore, one of ordinary skill in the art

upon reading Howe would not aspirate a preselected quantity of fluid from a first aspiration zone in the container, wherein the preselected quantity of fluid is less than 1/2 (one-half) the volume of fluid in the container, and aspirate the fluid from the second aspiration zone whereby the magnetic particles are separated from the fluid, as is claimed in the present application, because such would not result in the resuspension of the particles in a liquid as disclosed by Howe. Rather, the claimed method of separating particles from a fluid results in a high capture of particles in the container, which reduces the loss of the particles to the aspirated fluid.

Kreuwel discloses removing the washing liquid from the container in a single aspiration step. In addition, once a volume of elution buffer has been added to the container (about 0.2 milliliters), Kreuwel discloses removing substantially all of the elution buffer from the container in one aspiration step to reduce the volume of elution to a required volume (e.g., 10-50 microliters). This is done to reduce the amount of elution buffer in the container, which is required to be a small quantity in order to concentrate the nucleic acid target (see page 7, l. 40 – page 8, l. 14, Fig. 4). In other words, Kreuwel teaches a single aspiration step to remove a large volume of elution buffer, which is more than one-half of the elution buffer in the container, and which must be removed in order to reduce the buffer to a smaller quantity required for further processing of the fluid.

Conversely, the present invention aspirates a preselected quantity of fluid from a first aspiration zone, which is less than 1/2 (one-half) the volume of fluid, and aspirates the fluid from a second aspiration zone in order to reduce the loss of particles from the container during aspiration. Therefore, one of ordinary skill in the art after reading Kreuwel would not aspirate a preselected quantity of fluid from a first aspiration zone in the container, wherein the preselected quantity of fluid is less than 1/2 (one-half) the

volume of fluid in the container, and aspirate the fluid from the second aspiration zone whereby the magnetic particles are separated from the fluid, as is claimed in the present application. It is respectfully submitted that this is simply not disclosed by Kreuwel. It is also respectfully submitted that one of ordinary skill would not utilize the claimed method in Kreuwel because Kreuwel is not concerned with high capture of particles during separation of particles from fluid, which reduces the loss of the particles during aspiration of the fluid from the particles. Rather, Kreuwel is concerned with reducing the volume of elution buffer in a single aspiration step so that further processing may be conducted.

With respect to both Howe and Kreuwel, it is clear the Examiner has used hindsight reasoning and taken Applicants' claim as a blueprint to reconstruct the features of claim 1 from the prior art without regard to the fact that the prior art made of record is completely devoid of two aspiration steps to separate magnetic particles from the fluid, in which the preselected volume is less than 1/2 (one-half) the volume of the fluid. Such a teaching is not disclosed, taught, or suggested by the prior art made of record. Furthermore, such a teaching is in conflict with the prior art, which discloses removing fluids from containers in a single aspiration step, adding and removing resuspension liquid to resuspend particles (Howe), and removing greater than one-half (i.e., substantially all) of the fluid from the container in one aspiration step in order to reduce the fluid to a smaller volume required for additional processing (Kreuwel). Therefore, Applicants respectfully request withdrawal of the above rejection, and respectfully submit that claim 1 is allowable over the prior art made of record.

The Examiner rejected claims 15-17 as anticipated by Howe and Kreuwel. With respect to amended claims 15-17[1] and newly added claims 22 and 31, the claims recite a

[1] Claim 17 is not currently amended, but includes the method of separating magnetic microparticles in a fluid recited in claim 16. Thus, discussion related to claim 16 also applies to claim 17.

method for separating magnetic particles in a fluid that includes, among other things, placing or positioning the container and magnet or magnets in a first position relative to one another, aspirating or actuating a pipette to aspirate a preselected quantity of fluid, placing or repositioning the container and magnet or magnets into a second position relative to one another distal from the first position,[2] and aspirating or actuating a pipette to aspirate a portion of the fluid. As amended, the step of placing or repositioning the container and magnet or magnets into a second position, and the second recited step of aspirating are conducted "without adding fluid to the container," or as recited in claim 31, "before adding additional fluid to the container." Thus, the invention utilizes multiple magnet particle capture steps with aspiration of the fluid between each capture step, i.e., intermittent or intervening aspiration, to separate magnet particles from the same fluid. In this way, as discussed above with respect to claim 1, the present invention performs a volume reduction in a single container in a timely fashion, while ensuring high capture of particles for subsequent steps that are completed at relatively low volumes. The present invention allows more effective evacuation of fluid from the container, and the high capture of particles reduces the extent of magnetic particle loss during the aspiration of the fluid from the container.

Neither Howe nor Kreuwel disclose, teach, or suggest positioning the container and magnet or magnets in a first position, aspirating a preselected quantity of fluid from a first aspiration zone, and without adding fluid in the container, positioning the container and magnet or magnets into a second position distal from the first position, and aspirating the fluid from a second aspiration zone to separate the magnetic particles from the fluid. Likewise, claim 31 recites the separation stages occur before adding additional fluid to the

[2] While claim 16 defines the location in a different way, the result is the same, the second position is distal from the first position.

container. In other words, the aspiration and positioning or placing steps of the present invention are conducted on the **same** fluid, but at different locations within the container. Conversely, Howe discloses a single aspiration step to remove the supernatant fluid from the container. Thereafter, Howe discloses resuspending the magnetic particles left behind in the container by adding a different fluid, i.e., a resuspension liquid to the container to resuspend the particles in this new liquid. Applicants respectfully submit that the current claims as amended and newly presented overcome the rejection over Howe. Therefore, Applicants respectfully request withdrawal of this rejection.

Similarly, Kreuwel discloses removing the wash solution from the container, adding an elution buffer, i.e., a different fluid than the wash solution, then removing substantially all of the elution buffer after the magnetic particles are positioned at the extreme bottom of the container. At the extreme bottom of the container, the buffer and particles are heated to activate the buffer. After heating, the magnetic particles are dragged upwards toward the open end of the container above the surface of buffer to physically separate the particles from the buffer.

The present invention, on the other hand, recites positioning or placing the container and magnet or magnets in a first position, aspirating a preselected amount of fluid, and without adding fluid to the container, repositioning or placing the container and magnet in a second position distal from the first position, and aspirating a portion of the fluid to separate the magnetic particles from the fluid. While Kreuwel discloses dragging the particles slightly upwards in the container, the present invention recites the exact opposite. In addition, Kreuwel discloses dragging particles downward to the extreme bottom of the container before aspirating. Therefore, Kreuwel is incapable of repositioning or placing the container and magnets relative to one another in a second position distal

from the first position. Conversely, the present invention aspirates the fluid intermittently as the container and magnets are placed or positioned in a first position, then repositioned or placed in a second position distal from the first in order to ensure high capture of particles to reduce loss of the particles from the container during aspiration. Applicants respectfully submit that the current claims as amended and newly presented overcome the rejection over Kreuwel. Therefore, Applicants respectfully request withdrawal of this rejection, and respectfully submit that claims 15-17, 22, and 31 are in condition for allowance.

With respect to newly added independent claims 26, 30, and 32, the claims recite, among other things, that the container and magnet or magnets are placed or positioned in a first position, a preselected quantity of fluid is aspirated from a first aspiration zone so that a remaining quantity of fluid is left behind in the container, the container and/or magnet or magnets are placed or repositioned into a second position distal from the first position, and at least a portion of the remaining quantity of fluid is aspirated from a second aspiration zone to separate the magnetic microparticles from the fluid. Thus, the aspiration steps are conducted on the **same** fluid held in the container at different locations, which in turn acts to ensure high capture of particles and reduce the loss of particles during separation of the fluid from the magnetic particles. As discussed above, the prior art made of record fails to disclose, teach, or suggest separating magnetic particles from fluid using at least two aspiration steps on the **same** fluid in the locations claimed. Rather, the prior art made of record discloses a method which utilizes a single aspiration step to remove a fluid from a container, and then subsequently adds additional fluid to the container before that fluid is removed from the container. Therefore, Applicants respectfully submit that new claims 26, 30 and 32 are in condition for allowance.

With respect to claims 17 and 32, the prior art made of record fails to disclose, teach, or suggest, the method steps related to separating magnetic microparticles from a fluid suspension comprising a sample, lysis solution, and magnetic microparticles in combination with the other steps related to the washing solution and elution buffer. In addition, with respect to claim 17, the prior art made of record fails to disclose raising the container relative to the magnet such that the bottom of the container is raised above the top of the magnet in combination with the other features claimed. Therefore, Applicants respectfully submit that claims 17 and 32 are in condition for allowance.

Dependent claims 18, 19-21, 23-25, 27-29, depend from claims 1, 15, 22, and 26 respectively. For the reasons given above, Applicants respectfully submit that these independent claims are allowable over the prior art made of record. Accordingly, Applicants respectfully submit that these dependent claims are also allowable over the prior art made of record.

CONCLUSION

In view of the foregoing amendments and remarks, Applicants respectfully submit that the claims in the application are in allowable form and that the application is now in condition for allowance. If, however, any outstanding issues remain, Applicants urge the Examiner to telephone the Applicants' attorney so that the same may be resolved and the application expedited to issue. Applicants respectfully request the Examiner to indicate the claim as allowable and to pass the application to issue.

Respectfully submitted,

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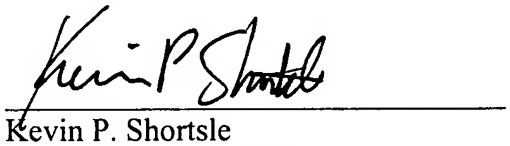

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